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Review article

Hydrolyzed collagen: Exploring its applications in the food and beverage industries and assessing its impact on human health – A comprehensive review

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ABSTRACT

Hydrolyzed collagen (HC) consists of many small and low-molecular-weight amino acid chains (3–6 kDa) that can be produced either in basic or acidic media through enzymatic activity. This review details the sources of hydrolyzed collagen, its biosynthesis and its uses in the food industry, as well as its production process and beneficial health effects. HC can be extracted from a variety of sources, during which acetic acid is used for the extraction of collagen type I from bovine, porcine, marine, chicken, and fish cartilage. An enzymatic treatment combined with an acidic treatment has shown more efficient extraction results. Because of its properties, it is frequently employed in the food industry since it improves sensorial qualities, as well as in the cosmetic industry as a functional component in face and body cream because of its moisturizing properties. It is also used in the pharmaceutical development of antioxidant supplements often combined with hyaluronic acid and vitamin C. HC has an excellent therapeutic effect on osteoporosis and osteoarthritis, where a daily dose of 12 g enhances pain symptoms and contributes to bone health. It also increases mineral density and protects articular cartilage. This review presents the structure and properties of hydrolyzed collagen, which mainly consists of the amino acids glycine, proline and hydroxyproline in a triple helix, its extraction process and its sources, as well as its applications. In particular, the creation of Enzymatic Membrane Reactor allows the production of HC with different molecular weight distributions, allowing wider application.

1. Introduction

Collagens are insoluble structural proteins that are heterogeneous in terms of their properties, location, spatial and molecular structure. Collagen is the most prevalent and ubiquitous protein in the animal kingdom and can be found in animal skin, bone, cartilage, tendons, blood arteries, and many other connective tissues. The composition and structure of the fibers that make up this

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protein determine its function. Tropocollagen is the basic building block of collagen that makes up collagen fibers; it is made up of three coiled left-handed polypeptide strands. Glycine and proline are the most common amino acids in collagen polypeptide chains [1].

Many cells in the body continually produce different amounts of collagen on demand. Collagen is primarily synthesized in fibroblasts found in connective tissues. Several posttranslational modifications occur after collagen is synthesized either intracellularly or extracellularly [2]. Thermal treatment (above 40 °C) causes native collagen to denature, resulting in three random coiled chains. After the denaturation of collagen, hydrolysis occurs using proteolytic enzymes, resulting in the formation of hydrolyzed collagen (HC) as the final product [3]. Bovine and porcine tissue are the major sources of collagen because of their wide availability and biocompatibility with human tissues. It has a broad range of applications and is allergen-free. Many alternative sources have been developed as a result of this feature, including fish tissues, fish byproducts, chickens, and other animal sources [4]. HC is a commonly used, effective ingredient in food, cosmetic, biomedical, and pharmaceutical manufacturing. It has antioxidant and antimicrobial capacities and does not affect the sensory properties of food. It is usually used as a promising functional ingredient to ameliorate the physicochemical and effective properties of a variety of food products [4].

Hydrolyzed collagen plays therapeutic and restorative roles in osteoporosis and osteoarthritis [5], minimizing fine and deep facial lines, improving the hydration and elasticity of the skin [6], lowering the risk of heart disease [7], and being involved in the process of wound healing and repair [8].

Hydrolyzed collagen is prepared by breaking down large native collagen proteins into smaller peptides, which are easier for the body to absorb. This process, known as hydrolysis, can be achieved either enzymatically or chemically. Enzymatic hydrolysis is often favored for its specificity and mild conditions, and proteases such as pepsin, trypsin, or alcalase are used to cleave the peptide bonds within collagen. Alternatively, chemical hydrolysis uses acids or alkaline solutions to achieve a similar effect. The choice of method affects the molecular weight and bioactivity of the resulting hydrolyzed collagen, impacting its solubility, antioxidant properties, and ease of use in various products ranging from dietary supplements to cosmetics.

This review aims to explore the extraction methods and functional applications of hydrolyzed collagen, demonstrating its potential use in the food and nonfood industries. The structure, characteristics, and properties of collagen proteins are briefly described. It focuses on the properties of hydrolyzed collagen, its extraction process, and its sources. This study sheds light on the food and nonfood applications of hydrolyzed collagen. This explains the health and beneficial effects of hydrolyzed collagen and demonstrates its antioxidant and anti-inflammatory capacities [9].

2. Collagen, structure, characteristics, and properties

Collagens are heterogeneous polymers and insoluble structural proteins that differ in their properties, location, and spatial and molecular structure. The collagen family is differentiated by mechanical strength resulting from the wide structural differences, occurrence, and function of protein members. It is the major protein of the skin, tendons, ligaments, cartilage, and bones and is the principal insoluble fibrous protein in the extracellular matrix of connective tissues; it provides them with integrity, strength, and elasticity. The role of this protein relies on the specific structure of the fibers it is made of. It is crucial for tissue growth, regeneration, and wound healing, as well as for cell adhesion and differentiation. Tropocollagen is the fundamental structural unit of collagen that makes up fibers. It is composed of three left-handed polypeptide chains coiled around each other. Tropocollagen molecules aggregate with each other through electrostatic and hydrophobic interactions, forming collagen fibers. Some collagens have helical and nonhelical domains. Fibrils among polypeptide chains interact with each other in a manner that determines the structure and function of collagen. The amino acids interact and pair with each other by covalent and noncovalent bonds, forming trimers. Different types of collagen have different polypeptide chain compositions, and some may share structural similarities, including identical homotrimers or heterotrimers [10]. Collagen polypeptide chains are mostly composed of glycine (35 %) and proline (12 %). Lysine (Lys), arginine (Arg), alanine (Ala), aspartate (Asp), and glutamate (Glu) rarely occur in the polypeptide chains of collagen, while hydroxylysine (Hyl) and hydroxyproline (Hyp) can be found in chains at significant concentrations when highly ordered collagen structures are formed. Both basic and acidic amino acids occur in collagen polypeptide chains with an equal number of moles. The spatial structure of collagen is modulated by repeated sequences of amino acids, where the most repeated amino acid sequence is Gly-Pro-X and the second most common sequence is Gly-X-Hyp. The letter X refers to any of the 17 other amino acids [2]. However, the less common amino acid sequence is Gly-Pro-Ala [1]. Gly is usually present in systematic order and allows for the formation of hydrogen bonds between molecules. This regularity and consistency of amino acid sequences together with the surrounding aqueous medium provide collagen with an entire helical structure with strength, stability, and flexibility. This implies that the more kinks and twists there are in the polypeptide chain, the less regular the amino acid sequence is. The elasticity of the collagen molecule is determined by this relationship [1].

2.1. Collagen family

There are 28 known types of collagen, and they are classified according to their different structures, locations, and properties. The 28 different types are distributed among the individual body and play substantial roles in many tissues, including skin, bones, cornea, vessels, gristles, intestines, glands, heart, kidneys, brain, and skeletal muscles [1].

Fibrillar collagen and nonfibrillar collagen are the two main groups of the collagen family. Most of the proteins in the extracellular matrix of vertebrates are fibrillar collagens, which constitute approximately 90 % of all collagens present in the human body, providing tissues and organs with structure, stability, and connectivity. Collagens types I, II, III, V, XI, XIV, and XXVII are classical fibrillar collagens [9]. The three helically rolled polypeptide chains are encoded by eleven genes and are separated by teleopeptides (short nonhelical fragments). Fibrillar collagens are derived from repeated sequences of Gly-Pro-Hyp residues in the alpha chains. Then, these triple helices self-assemble into thick and thin fibrils. Disturbances in the Gly-X-Y repeated sequences of the alpha chains cause the formation of nonfibrillar collagens [11]. Non-fibrillary collagens account for only 10 % of the total collagen present in the human body. They differ from fibrillar collagen in terms of their structure, location, and properties. These collagens can be categorized as anchoring collagens, basement membrane collagens, microfiber building collagens, network system collagens, membrane-associated collagens with interrupted triple helices (MACITs), fibril-associated collagens with interrupted triple helices (FACITs), and multiple triple helix domains and interruptions (Multiplexins) [4]. The presence of several molecular isoforms, α chains, and supramolecular structures for a collagen type, as well as the utilization of different splicing products and promoters, all increase the diversity among collagen proteins [1,9].

Collagen proteins can be affected by temperature, leading to denaturation in two steps. First, the hydrogen and hydrophobic bonds within the helical structure are degraded. In the second step, the helical structure is denatured and converted into a globular structure. The factors that affect the process of collagen denaturation are temperature, pH, salt concentration, electrolytes, and the amount of hydroxylproline [1,10].

Collagen responds to thermal treatment by changing its consistency, viscosity, and plasticity. The molecular structure of collagen protein is responsible for its physiochemical properties. As collagen fibers age, crosslinking increases, and the resistance to mechanical force increases. The integrity of the tissues is guaranteed as crosslinking increases so that collagen can bind the elements of the extracellular matrix well. Nevertheless, collagen is insoluble in water and resistant to proteolytic enzymes because of its helical spatial structure and its ability to hold water [1,10].

2.2. Collagen Biosynthesis and Biodegradation

2.2.1. Collagen biosynthesis

Various cells in the body continuously produce various amounts of natural collagen biopolymers in response to demand. This protein is synthesized mainly in fibroblasts within connective tissues. Collagen synthesized either intracellularly or extracellularly undergoes several posttranslational modifications [2].

At the intracellular level and starting in the nucleus, the transcription of mRNA occurs where genes encoding the pro-α1 and pro-α2 chains are transcribed. The mRNA is then moved toward the cytoplasm to undergo translation into a prepro-polypeptide chain. Preprocollagen consists of a signal peptide fragment that recognizes the polypeptide molecule and then transports it to a suitable place in the ER, preventing the premature formation of collagen fibrils [1]. Preprocollagen undergoes three major posttranslational modifications in the endoplasmic reticulum (ER). The signal peptide attached to the N-terminus of the chain is removed. This process is then followed by proline and lysine residue hydroxylation using the hydroxylase enzymes prolyl-4-hydroxylase, lysine hydroxylase, and prolyl-3-hydroxylase. Molecular oxygen, ascorbic acid, α-ketoglutarate, and iron ions (II) are necessary for this phase [2]. During posttranslational modifications, hydrogen bonds are important for the stabilization of the spatial structure of the protein. At the final step of posttranslational modifications, the hydroxyl groups on lysine undergo galactose and glucose glycosylation in the presence of glucosyl-transferase and galactosyl-transferase. A zipper-like folding left-handed helix formed when three hydroxylated and glycosylated pro-a-chains assembled and twisted into a right-handed coil. Final modifications take place in the Golgi apparatus, where pro-collagen is enclosed in secretory vesicles and stabilized by hydrogen and disulfide bonds to enter the extracellular space [2].

At the extracellular level, collagen peptides carry out propeptide cleavage and eliminate the ends of procollagen molecules, converting them into tropocollagen using N-proteinase and C-proteinase. Lysines and hydroxylysines undergo oxidation by the Lysyl oxidase enzyme. Then, the collagen fibril is assembled spontaneously by covalent bonding between tropocollagen molecules, ending with the formation of collagen fibrils, which is the last step in the production and synthesis of the collagen protein [1,2].

2.2.2. Collagen biodegradation

At the intracellular level, collagen proteins are degraded by phagocytes (through endocytosis). Then, the peptide bonds between neighboring amino acids (Gly-Isl and Gly-Lys) are disrupted using enzymes (MMPs) at the extracellular level. This induces total destruction of the collagen triple helix. The process of degradation ends with two collagen disintegration products with a ratio of 3:1 that then undergo denaturation to become water-soluble molecules [1]. Collagenases and proteases as well as elastases play a significant role in the process of collagen degradation. Collagenases act at neutral pH and cleave molecules at specific loci across polypeptide chains on the surface of fibrils. On the other hand, proteases have a symbiotic effect on the degradation of both collagen fibers and fibrils by cleaving peptide bonds in telopeptide regions [12]. Both collagen synthesis and degradation are conditioned by environmental factors, where the precursor of collagen can be stimulated by mechanical stress [1,9].

2.3. Role of collagen in the human body

Collagen intervenes in many biochemical processes and promotes cell signal transmission, proliferation, and migration when it binds to integrins and other mediator proteins. Collagen interacts with proteoglycans to provide tissues with the required strength. The production and breakdown of collagen are controlled by various collagens, such as collagenases and chaperones [13].

Collagen plays a crucial protective *role in* humans. It interferes with neoplastic cell formation, metastasis, and angiogenesis. It is also involved in tumor microenvironment development and may suppress the immune signals that inhibit the antitumor immune response. Collagen improves the function and performance of the immune system because it binds to the C1r and C1s proteases, the enzymes that are responsible for triggering an immunological response and turning on the immune system. Collagen can bind and receive different ligands to achieve a specific function in the body. It can bind polyanionic compounds such as LDL and therefore lower the LDL concentration in the blood. Collagen plays an important role in wound healing due to its chemotactic role [1,10].

There are numerous roles and functions of collagen proteins. It has a spatial structure and high molecular mass. Collagen protein has limited applications when it is used in solution because it has poor solubility in water. A soluble form of collagen can be extracted by hydrolysis with better properties, such as good water solubility and less molecular weight. Hydrolyzed collagen can be effectively used in the production of food and beverages, the design of many dietary products, the pharmaceutical industry, and many other applications. Hydrolyzed collagen is prepared from a denatured protein to be more easily absorbed and digested in the human body [13].

3. Hydrolyzed collagen

3.1. Sources of hydrolyzed collagen

Porcine and bovine collagen are the major sources of native collagen because of their wide availability and biocompatibility with human tissues. Collagen can be extracted from connective tissues such as bones and tendons. Its usage is extensive, and it has no allergenic limitations. Because of these attributes, many alternative sources have been developed, including fish tissues, fish byproducts, chickens, ducks, and rabbit skins [4]. Enzymes produced by *Penicillium aurantiogriseum cacteria*, such as pepsin, trypsin, alcalase, and collagenase proteolytic enzymes, are usually used in the process of bovine collagen extraction [14]. Bovine collagen extracts have antioxidant and antibacterial properties [4]. On the other hand, porcine collagens are extracted by a hydrothermal process, where high pressure (350–3900 KPA) and temperature (150–250 °C) are involved. The extracted collagen was then fractionated using an ultrafiltration membrane. This source results in low-molecular-weight (1–10 kDa) hydrolyzed collagen with good antioxidant and anti-aging capacities [15]. High temperatures and pressures are involved in this extraction to obtain the very low molecular weight collagen peptides (15 kDa) that are commonly used in dietary supplements [4].

Many health disorders, such as bovine spongiform encephalopathy and swine flu, can be caused by traditional sources of hydrolyzed collagen. This has shifted the attention of researchers toward marine sources such as fish, jellyfish, and sponges as alternative sources of collagen extraction. Extraction parameters such as temperature, pressure, and the type of marine source (fish type or fish tissue) can affect the molecular weight of the extracted collagen peptides and their functional properties. Even marine byproducts can be employed as a reliable supply of hydrolyzed collagen or functional bioactive collagen peptides [4].

Compared with mammalian-extracted collagen, fish-extracted collagen has many advantages, including the ability to be purified and extracted, a reduced risk of disease transmission, a lack of religious and cultural boundaries, a more straightforward extraction method, greater adaptability and high metabolic compatibility, and reduced viscosity [16].

Alternatively, hydrolyzed collagen can be extracted from poultry legs by an enzymatic process in which the papin protease is involved at different temperatures and extraction intervals. Furthermore, the extracted collagen can retain oil and water and can function as an emulsifying and foaming agent [17].

3.2. Extraction and structure of hydrolyzed collagen

Native collagen undergoes denaturation when exposed to thermal treatment (above 40 °C), which produces three random coiled chains. The process of denaturation is then followed by proteolytic enzyme hydrolysis, resulting in hydrolyzed collagen (HC) as the final product [3]. Hydrolyzed collagen consists of many low-molecular-weight small peptides (3–6 kDa) (Fig. 1). Usually, the type of proteolytic enzyme utilized, along with the degree and type of hydrolysis, controls the product's solubility and functional antioxidant or antimicrobial properties [18]. Collagen hydrolysis can be conducted either by enzymatic action or chemically in acidic or basic

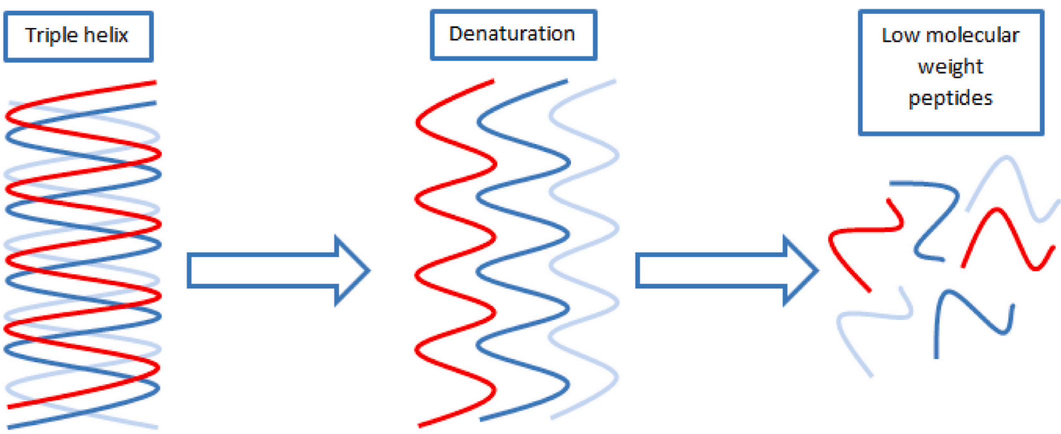

Fig. 1. Denaturation of native collagen protein into small peptides with a low molecular weight.

media. Both acidic and alkaline hydrolysis are strongly corrosive and contribute to a final product with high salt concentrations. Thermal treatments at elevated temperatures and pressures can be applied as alternative solutions [4].

3.2.1. Molecular weight assessment of collagen peptides

The molecular weight of the obtained hydrolyzed collagen can be determined using SDS−PAGE (Sodium Dodecyl Sulfate - Polyacrylamide Gel Electrophoresis) by separating the peptides in the mass range of 1–100 kDa. This method depends on the charge of the separated molecules.[4] Another technique used when the range of peptide molecular weights is very large is matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). In this method, the peptides are combined with an extensive molar excess of matrix, such as 2,5-dihydroxybenzoic acid, and then this matrix is vaporized to determine the mass of the final peptides produced from the ionic time of flight. The issue with this method is that some peptide peaks are unable to combine with the matrix being employed. HPLC-MS/MS is an appropriate technique for identifying and quantifying peptides and proteins, but it is primarily used for the measurement of a small number of biologically important peptides, such as collagen. Amino acid analysis is typically used to determine collagen types [19].

3.2.2. TNBS (trinitrobenzenesulfonic acid) method

The TNBS (trinitrobenzenesulfonic acid) method is a widely used analytical technique to measure the degree of hydrolysis of protein samples, including hydrolyzed collagen. This method involves quantifying the free amino groups that are exposed in a protein when peptide bonds are cleaved during hydrolysis. When TNBS reacts with these free amino groups, it forms a measurable yellow–orange complex. The intensity of this color, quantified through spectrophotometry, is directly proportional to the concentration of free amino groups, thus providing an index of hydrolysis [20]. To validate the reliability and accuracy of the TNBS method, various studies have been conducted. For instance, research has shown that the TNBS method can effectively differentiate between varying degrees of protein hydrolysis and correlates well with other analytical techniques, such as HPLC or gel electrophoresis, for detecting peptides and amino acids. This method is particularly favored for its simplicity, sensitivity, and cost-effectiveness, making it suitable for routine analysis in research and industrial settings. Moreover, the functionality of hydrolyzed collagen, which often relates to its molecular size distribution and the presence of specific peptides, has been linked to the degree of hydrolysis, as measured by the TNBS method. Studies have indicated that certain functional properties, such as antioxidant activity or bioavailability, can be correlated with TNBS measurements, providing a valuable tool for optimizing and controlling the production processes of hydrolyzed collagen [21,22]. On the other hand when comparing TNBS method to other methods, it proved its efficiency and since TNBS binds strongly to cysteine, this technique was deemed more suitable when preparing whey proteins hydrolysates to quantify the degree of hydrolysis [23].

4. Technical aspects of collagen hydrolysis

4.1. Hydrolyzed collagen production

Hydrolyzed collagen is made from the same raw materials as traditional gelatin, which is made by denaturing and partially hydrolyzing collagen. Collagen and its hydrolyzed form are commonly made from pig or cow skin. However, mad cow disease and the religious ban on pork skin and bone collagen in some areas have necessitated the search for new marine or fowl sources that are safer for consumers. Chemical or enzymatic hydrolysis are two methods for obtaining hydrolyzed collagen. Although many manufacturers

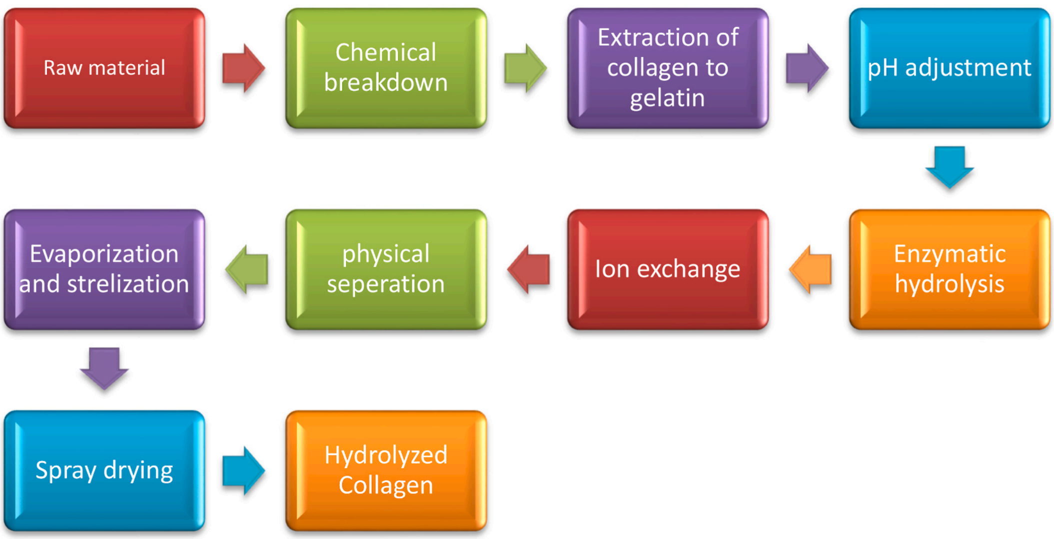

Fig. 2. The general procedure for producing hydrolyzed collagen using a combined method, modified from [24].

still use chemical hydrolysis, the enzymatic hydrolysis of proteases is the preferred method because it is more controllable [24]. Because of the stable triple helix, enzymes have difficulty digesting the collagen domain, but denatured gelatin is quickly tracked by proteinases [25]. A combination of enzymatic and chemical hydrolysis methods is often used. The manufacturer first prepares the gelatin by chemical hydrolysis, which is then hydrolyzed by enzymes until the desired molecular weight is reached. Commercial gelatin has recently been used as a starting material in a new process to produce collagen hydrolysate in a shorter time [24].

Dietary proteins are often refined and enhanced through enzymatic hydrolysis. There are many types of enzymes. Protease enzymes are suitable for the hydrolysis of gelatin into hydrolyzed collagen. To achieve more selective hydrolysis, proteases from various sources are frequently utilized since they have a preference for peptide bonds adjacent to particular amino acid residues [24].

Trypsin, pepsin, chymotrypsin, bromelain, pancreatin, papain, Alcalase, Prophase E, Flavorzyme, Neutrase, and Protamex are commercial proteases that have been used to produce collagen hydrolysate. Microbial alcalase is widely used due to its broad specificity and high ability to achieve hydrolysis in a short time [26]. Substrate concentration, enzyme-to-substrate ratio, temperature, and pH are the parameters of hydrolysis. These four hydrolysis parameters are the main determinants of the enzymatic reaction rate [24]. The general process for producing hydrolyzed collagen using a combination of chemical and enzymatic hydrolysis is illustrated in Fig. 2, while the general process for producing hydrolyzed collagen using commercial gelatin as the starting material is illustrated in Fig. 3. The molecular weight of the hydrolyzed peptides is one of the most essential factors in achieving the necessary functional qualities of the produced hydrolyzed peptides. During the separation process, an advanced membrane filtration technique can be used to fractionate the hydrolyzed peptides. Membranes reduce energy consumption while also potentially saving water through recycling. The use of an ultrafiltration system to obtain hydrolysate fractions with an appropriate molecular size could be a useful and positive industrial method [27].

4.2. *Effect of technical parameters on the quality of hydrolyzed collagen*

The production of hydrolyzed collagen involves precise control of several key variables, including temperature, pH, enzyme selection, and reaction time. Each of these factors significantly influences the characteristics and quality of the final product, such as its molecular weight, solubility, and bioactivity.

4.2.1. *Temperature*

Temperature is a critical factor in the enzymatic hydrolysis of collagen. The enzymes used in hydrolysis are sensitive to temperature changes; each enzyme has an optimal temperature range where its activity is maximized. For example, temperatures that are too high can denature the enzyme, reducing its effectiveness, while temperatures that are too low can result in inadequate reaction rates. Typically, enzymatic hydrolysis is performed at temperatures between 45 °C and 55 °C. This range helps to maintain enzyme activity and can also affect the rate of hydrolysis and the size of the hydrolyzed collagen peptides [27,28].

4.2.2. *pH*

The pH of the reaction mixture also plays a crucial role in the enzymatic hydrolysis of collagen. Each enzyme has an optimal pH at which it functions most efficiently. For instance, pepsin performs best under acidic conditions (pH 1.5 to 2.5), while trypsin is more effective in a slightly alkaline environment (pH 7 to 8). pH not only influences enzyme activity but also affects the stability of the collagen molecule itself, impacting the susceptibility of the resulting peptide bonds to enzymatic cleavage [17,18].

4.2.3. *Enzyme selection*

The choice of enzyme determines the specific sites on the collagen molecule where peptide bonds are cleaved, thus influencing the size and bioactivity of the resulting peptides. Different enzymes target different cleavage sites. Pepsin cleaves at hydrophobic residues, often producing larger peptides. Trypsin targets basic residues such as lysine and arginine, typically resulting in smaller peptides with different functional properties. Alcalase, a more nonspecific protease, produces a wide range of peptide sizes and can enhance the solubility and antioxidant activity of hydrolyzed collagen [14,29].

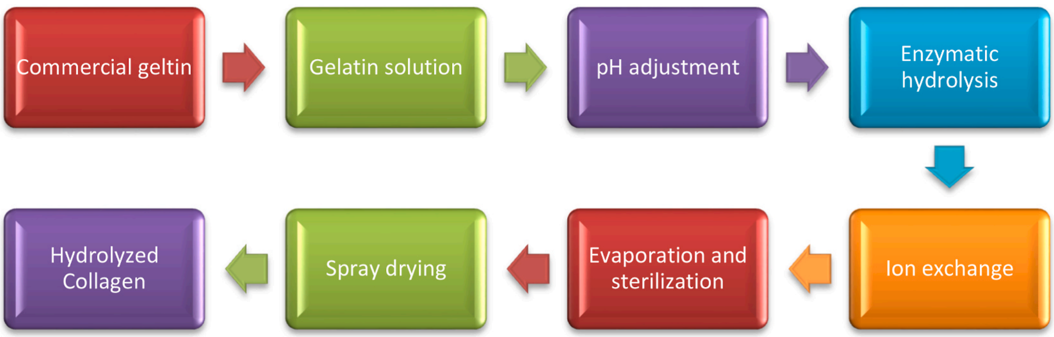

Fig. 3. The general procedure for producing hydrolyzed collagen with commercial gelatin as a raw material, modified from [24].

4.2.4. Reaction time

The duration of the hydrolysis reaction significantly impacts the degree of hydrolysis and the molecular weight distribution of the collagen peptides. Longer hydrolysis times generally increase the degree of hydrolysis, resulting in smaller peptides with potentially higher bioactivity and better solubility. However, excessively long reaction times might lead to the breakdown of beneficial peptides into amino acids, reducing the functional benefits of the hydrolyzed product [24,26]. Each of these factors must be optimized to produce hydrolyzed collagen with desired properties suitable for specific applications, whether in food, cosmetics, or pharmaceuticals. Proper control of these parameters ensures that the hydrolyzed collagen is not only effective but also consistent in quality.

4.3. Properties of hydrolyzed collagen

The characteristics of native collagen significantly differ from those of hydrolyzed collagen, as shown in Table 1. As a consequence of the disruption of hydrogen bonds when collagen is hydrolyzed, the native collagen triple-helix structure transforms into a random coil shape after denaturation. This process can breakdown polypeptide bonds to produce many peptides. The collagen peptides produced during hydrolysis have a much lower molecular weight (3–6 kDa) than their native protein precursor (285–300 kDa). The size of peptides and their biological and physicochemical characteristics are affected by the utilized hydrolysis enzyme [30]. Viscosity is one of the physicochemical qualities of collagen; the natural form is highly viscous due to increased electrostatic repulsion between molecular chains. Protein electrostatic characteristics, including the isoelectric point (pI), are cardinal parameters that are linked to the amounts of acidic and basic amino acids in the protein. Collagen is considered an amphoteric macromolecule with a pI ranging from 7 to 8. The pI was adjusted to between 3.68 and 5.7 throughout the hydrolysis process. The distribution of amino acid residues among the amino acid sequence will change depending on the time of hydrolysis and the hydrolysis type. The functional properties of collagen, such as its antioxidant capability, bioavailability, and antibacterial activity, are influenced by its composition and degree of hydrolysis. The molecular weight mostly affects these features. It causes hydrolyzed collagen to behave as an electron donor to other molecules [4].

Native collagen is widely employed in a variety of industries because of its high biocompatibility and biodegradability, minimal immunogenicity, and adaptability in film fabrication. However, while hydrolyzed collagen is extremely soluble in water, it is incapable of forming films on its own. It must be combined with other biopolymers. Compared to native collagen, hydrolyzed collagen has various advantages. Some of them include efficiency in terms of cost and therapeutic loading and the lack of a multiple-step extraction technique, as well as being digestible and quickly absorbed and dispersed in the human body [31]. It also has a natural odor and transparent color, a decreased viscosity in aqueous solutions, emulsification and stabilization capacity, foaming and filming ability (if combined with a biopolymer), and low allergenicity. Powdered HC is a highly soluble and compressible material that has excellent wettability and dispersibility and can act as a good carrier material. As a consequence, collagen peptides can be employed as functional food supplements [4].

The quality of the collagen peptides relies on the extraction process. These peptides can bind calcium ions, increasing their bioavailability and making them more compatible with the human body. *In vivo* studies have demonstrated that hydrolyzed collagen helps to promote memory health; therefore, it might be a potential component of pharmaceutical products used to maintain and enhance human health. It has great potential for use in food that requires freezer storage since it reduces or prevents damage to cells and tissues caused by storage at very low temperatures [4].

5. Applications of hydrolyzed collagen in food and nonfood industries

Collagen properties can be classified into two categories. First, the capacity of collagen for thickening and texturizing, gel formation, and water binding capacity are some of the features associated with collagen gelling behavior. Collagen surface properties, such as emulsion, foaming, stabilization, adhesion and cohesion, the protective function of its colloid structure, and its film-forming capacity, are classified in the second category [27]. Collagen is also a good surface-active agent that has been shown to penetrate a lipid-free interface [32]. The ability of collagen proteins to self-aggregate and the formation of cross-links between polypeptide chains make them valuable in drug delivery systems. The wide use of collagen in drugs and pharmacology is due to its high biological compatibility and biodegradability, efficient antigenicity, low allergenicity, and hemostatic activity. These properties make it effective in the tissue engineering and film industries [33].

As part of its multiple use in biomedicine, hydrolyzed collagen serves as drug carrier, tissue engineering material, bone filling, enzyme immobilizer and burn and wound dressing. Since HC has a variety of usage, many of its resources are still under investigation

Table 1
Properties of undenatured and hydrolyzed collagen modified from (León-López et al., 2019).

Properties	Type of Collagen	
	Undenatured collagen	Hydrolyzed collagen
Molecular weight (Mw)	285–300 kDa	3–6 kDa
Isoelectric point (pI)	7.0 to 8.3	3.68 to 5.7
Viscosity	high	Low (0 Cp)
Ability of forming films	Yes	Needs biomaterial

* Cp stands for centiponents of absolute viscosity.

especially collagen from cows and pigs. For religious believes and diseases-related issues, mammalian based-collagen is still limited. To serve as a biomaterial design, the starting material has to be similar to an already existing one, and fish collagen has been under intensive research for many years now for being a good potential [34].

Since collagen is biodegradable and easily absorbed in the body, it serves as a drug delivery system under several applications such as nanoparticles for gene delivery, pellets for the delivery of proteins, aqueous injection for the treatment of cancer as well as many other applications in ophthalmology [35]. Conventional drug delivery systems show side effects in some cases, while smart DDS improve therapeutic efficacy by providing a regulated and prolonged release. On the other hand, tissue engineering is based on using a combination of cells with physiochemical and biochemical properties that enables the renewal of different types of biological tissues [36].

Hydrolysis of collagen is optimized in many conditions in order to expand its use in industrial applications. To do so, many techniques can be applied of which response surface methodology used to optimize hydrolysis conditions of collagen from yellowfin tuna skin that resulted in Collagen hydrolysate, rich in hydroxyproline residues, methionine, glycine and proline. This hydrolysate can be thus used in many functional food products since it has an excellent antioxidant power, a good inhibition rate of oil oxidation and anti-freezing properties [37]. On the other hand, the enhanced physiochemical properties of collagen derived from bovine limed split wastes had allowed it to be used in many applications as biomaterial and additive [38].

5.1. Collagen peptides in Food and beverage industries

Currently, collagen is a very popular ingredient used in the development of healthy foods. With age and a poor diet, the body's collagen production decreases. Because most people do not like to receive collagen injections, the best way to obtain collagen is through diet. Collagen has thus been added to a number of foods and drinks. Local retailers offer a wide range of commercial collagen products from different suppliers. A few examples of food-grade bovine collagen are Colageno from the JBS Brazilian Company and Cosen from the Chinese Jiangxi Cosen Biochemical Industry. Moreover, Ovinex is a food-grade ovine collagen produced by Hollista CollTech in Australia via an enzymatic process. Ni-Kollagen by Bionic Life Science in Malaysia and Peptan by Rousselot SAS in France are two other marine collagens that have been suggested for use in dietary supplements, functional foods, drinks, and confectionaries [32].

5.1.1. Food applications

HC has antioxidant and antimicrobial properties, making it a candidate functional ingredient for use in food supplements. Hydrolyzed collagens can attach calcium ions, increasing their bioavailability. As a result, HC can be used to treat mineral deficiencies. Because HC works as an anticoagulant and minimizes the damage that low temperatures exert on tissues and cells, it may be useful in the storage of foods that must be kept at freezing or very low temperatures. A wide variety of items, including meat products, drinks, and soups, have been prepared with HC. It aids in the enhancement and maintenance of their sensorial, chemical, and physical characteristics [4].

The quality of Frankfurt-style sausages was improved by substituting part of the pork backfat with hydrolyzed collagen. The capacity to hold water increases with increasing hydrolyzed collagen concentration, as does product stability after heating and, therefore, textural characteristics such as hardness and chewiness. These elements influence consumer choice regarding the texture and flavor of the sausage. In addition, a greater fat reduction leads to additional nutritional advantages, such as a greater protein and mineral content, as well as a lower lipid content [33].

In the food industry, the rheological qualities of sausage and frankfurters are improved by the addition of collagens as a food additive. It maintains adequate levels of animal nutritive fibers and does not affect the sensory properties of sausage or frankfurters. To improve the quality of meat-based products, collagen is added to the liverwurst or paste to minimize the incidence of fat caps and layers [39].

Buffalo patties were also prepared with hydrolyzed fish collagen as a fat substitute. FCH has the potential to increase the protein content and decrease the fat content of patties without affecting the final meat product's cooking yield, WHC, shrinkage, sensory qualities, or overall acceptability [40].

Heat-treated collagen fibers have an excellent capacity to be used as emulsifiers in some acidic food preparations. Collagen can be used as a stabilizer for preparing emulsions with low protein content and low pH, maintaining a droplet size that is six times smaller than that of the primarily prepared emulsions by forming strong electrostatic forces between the dispersed droplets [41].

Herbal hydrolyzed collagen (HHC) soups were produced in retorts and stored in glass bottles as a functional, ready-to-serve beverage with health advantages. The retort procedure altered some of the physicochemical characteristics while boosting the antioxidative abilities of the resultant HHC soups. These HHC soups show excellent clarification, good sensory quality, and increased stability during storage, and they may promote collagen synthesis while also inducing cell proliferation [42].

Collagen has been used to replace lean meat in coarse and fine bologna. The pH of the pressed fluid, color, and cooking loss were all unaffected by collagen substitution [43]. The addition of collagen to sardine surimi improves its physiochemical properties, gel strength and hardness. Collagen can enhance the folding test score and maintain a desirable light color [44]. Hydrolyzed collagen has the potential to decrease syneresis in Turkey ham when used with nonmeat ingredients such as guar gum and starch [45].

Collagen is also used as an edible film and coating barrier membrane to prevent oxygen and moisture mobility while maintaining structural integrity and vapor permeability in food products. This effectively aids in increasing the shelf life of foods. Shrinkage during cooking was reduced, the juiciness of meat products was improved, and the removal of the elastic net after cooking or baking was made easier with edible collagen films that were suggested for use in hams, fillets, meat pastes, roast beef, netted roasts, and sausage casings

[39].

Hydrolyzed collagen shows great promise for use in baking materials. The addition of collagen peptides to bread products can enhance the bread's ability to retain water, increase bread-specific volume, and inhibit or delay bread staleness. Breads prepared with HC demonstrated a longer shelf life due to significantly decreased hardness and moisture loss [46].

5.1.2. Drinks applications

Drinks infused with collagen are now considered a popular trend on the worldwide market. Numerous items, including soy, cocoa, cappuccino collagen, collagen juice, and bird's nest drinks containing collagen, have been released by beverage manufacturers. Tree proposed a collagen-infused energy drink to support the body's natural production of fatty tissues. In general, the use of a collagen drink increases the body's production of collagen, promotes body tissues, and slows aging and the presence of wrinkle lines on the skin [39].

- In probiotic drinks, Malaysia Dairy Industries (MDI) delivers a probiotic collagen peptide drink infused with vitamin C. Collagen peptides are used as a component required for the synthesis of collagen, where vitamin C serves as a vital coenzyme required for this biosynthesis in addition to its antioxidation capacity. This drink was developed to encourage the proliferation of healthy gut bifidobacteria and to reinforce skin beauty and youthfulness [39].
- In alcoholic beverages, collagen is a clarifying component used in hazardous alcoholic beverages that works by aggregating yeast with other insoluble substances [25].
- Chemical modification makes bovine collagen solutions useful for beer refining and yeast preparations. Collagen has a strong caprylic flavor. However, blending 6 sucraloses and stevia extract with acesulfame potassium can significantly improve the taste of collagen-containing foods and beverages [39].
- Hydrolyzed collagen is used in dairy beverages and positively affects their physiochemical and sensory properties and boosts their microbiological capacity. It decreases syneresis and sedimentation in fermented dairy beverages and improves their physical, chemical, and microbiological capacities [4].
- HC has excellent clarification properties when used in Chrysanthemum beverages at the proper dosage and at ambient pH and temperature. It enhances the sensory quality of this drink product and improves its storage stability [47].

5.1.3. Collagen peptide supplementation

The health properties of collagen proteins have prompted the creation of collagen supplements. Collagen and its fractions have proven to be important nutritive ingredients in human diets due to their excellent moisture absorption qualities. Collagen synthesis decreases as people age, causing tissues to become thinner and weaker. Collagen supplements are designed to help users maintain healthy skin, nails, hair, and many other tissues. Collagen metabolites attract fibroblasts, which produce new collagen, which helps to build skin, bones, and ligaments. It increases the diameter of collagen fibrils in the dermis and dermal collagen fiber cohesion. As a result, tissue hydration, resilience, and supply will all improve.[34] It enhances the ability of the outermost skin layer to absorb water, and it could improve the dermal and epidermal functions of the skin. The hydration of skin tissue promotes smoothness and minimizes wrinkles [48].

Collagen supplements can help in gaining muscles with a very low amount of fat, reduce recovery time, repair joints, and improve cardiovascular performance. The production of creatine, an essential amino acid involved in the growth of new muscles after workouts, is promoted by collagen. Muscle mass is also aided by arginine, which is found in hydrolyzed collagen. Collagen is therefore in high demand in the world of sports nutrition [39]. In the dermis, hydrolyzed collagen acts in two ways. First, the free amino acids in hydrolyzed collagen serve as the elementary building blocks for the development of collagen and elastin fibers. In the second action, collagen oligopeptides function as ligands by attaching to receptors on fibroblast membranes and stimulating collagen, elastin, and hyaluronic acid production [4]. The applications of hydrolyzed collagen (HC) as a food supplement with a beneficial impact on the skin are shown in Table 2.

Table 2
Applications of hydrolyzed collagen (HC) as a functional supplement and its impact on the skin, modified from (León-López et al., 2019).

Product	Functionality	Duration	References
HC oral supplementation extracted from catfish skin	Enhance skin hydration, suppleness, and wrinkling.	(Tested on women 40–60 years old for 12 weeks).	[49]
Oral nutrient supplement with HC	Improved firmness, elasticity, and dermal thickness.	(Tested on women aged 35 to 65 for triple of months.	[50]
Fish-extracted oral HC supplement	Improve skin elasticity and texture, and maintains the health of joints	(Tested on 120 individuals for triple of months).	[51]
Fish-extracted oral HC supplement	Increase collagen density and moisture in the dermis	(Tested on women aged 40 to 59).	[52]
HC oral supplement with Vitamins E, C, A and zinc	Improve the firmness, elasticity, texture, and hydration of the skin	(Tested on women between the ages of 40 and 50 for 28 days).	[53]
HC drink	Development in the elasticity, moisture, and periorbital wrinkles of the skin	(Tested on healthy women between the ages of 30 and 60).	[54]
HC ampoules prepared with acerola fruit extract, vitamin C and E with zinc, and biotin	Elasticity, roughness, hydration, and density of the skin are improved	After 12 weeks of oral supplementation.	[55]

5.2. Nonfood applications of hydrolyzed collagen

Collagen is a safe and effective biomaterial because it is thought to be a good biocompatible and biodegradable material. It has recently been employed as a safe and efficient biomaterial in tissue engineering and medical applications. HC cannot produce scaffolds on its own, but it can do so when mixed with other biopolymers, such as cellulose and chitosan. The cellulose-HC blend used to create the films had excellent cell adhesion and proliferation support, good transparency, and good UV radiation absorption. The creation of an HC collagen biomaterial could be helpful for the treatment of bone and joint problems due to its low molecular weight and amino acid makeup. It is more bioavailable and promotes osteointegration, which increases collagen formation [4].

Chitosan sponges are alternative biomaterials to HCs. They are made using a sol-gel transition methodology, and the presence of HC results in a porous morphology, stability, good capacity for water uptake, good biocompatibility, and antimicrobial activity. Because HC has a lower water absorption rate than other materials, it has been utilized to create hydrogels for the administration of medicines such as methylene blue and insulin [56]. It is advantageous for medications that quickly disintegrate in the acidic, proteolytic environment of stomach juices. Chitosan and fish HC hydrogels were shown to have antibacterial effects on *Staphylococcus aureus* and *E. coli*, as well as on cell growth and migration and wound repair effectiveness. Nanofibrous scaffolds using HC as a regenerative component can be functionalized by electrospinning. It had a porous morphology, good mechanical strength, good biocompatibility, and antibacterial capacity against *Pseudomonas aeruginosa* and *E. coli*. [4] The applications of these HC biomaterials are illustrated in Table 3.

6. Health and beneficial effects of hydrolyzed collagen

6.1. Effect on skin

By reducing facial crinkle lines, maintaining water content inside skin tissues, and improving skin elasticity, HC supplements or collagen peptides can help to delay and improve signs of aging. Collagen hydrolysates are taken orally administered to promote fibroblast growth and stimulate the synthesis of new type I collagen in the dermis. It improves the texture of the skin by making it smoother and softer. The production of matrix metalloproteinase, the enzyme that is responsible for collagen degradation, is reduced when HC is consumed daily. The hydrophobic amino acids of the peptides account for the majority of HC antioxidant capacity [6].

In vitro studies have shown that blood peptides obtained from the ingestion of hydrolyzed collagen can induce the directional movement of skin fibroblasts, causing the migration and multiplication of murine fibroblasts. Collagen, hyaluronic acid, and elastin are produced by fibroblasts activated by hydrolyzed collagen. Collagen peptides can remain in the dermis for up to fourteen days after ingestion, protecting the skin from the sun and improving moisture retention while also assisting in the repair of endogenous elastin and collagen fibers. An improvement in skin aging was observed after oral intake of bovine-derived hydrolyzed collagen, as well as an increase in cutaneous protein and a change in the collagen type I to collagen type II ratio [62].

6.2. Effects on Osteoporosis and osteoarthritis

According to Moskowitz [63], the use of collagen hydrolysate in the treatment of bone diseases that cause joint pain and affect the function and mobility of joints, such as osteoarthritis and osteoporosis, has been evaluated. Products made from hydrolyzed gelatin have a long history of use in food and medicine, and regulatory organizations typically consider these products to be safe food products. The hydrolysis of pharmaceutical gelatin yields pharmaceutical-grade collagen hydrolysate (PCH). According to clinical research, people with hip or knee osteoarthritis who take 10 g of PCH daily report less pain, and their blood concentration of the amino acid hydroxyproline increases. Its clinical use is associated with minor side effects, mostly on the gastrointestinal tract of the digestive system, characterized by fullness or foul taste. As a potential therapeutic agent for the treatment of osteoarthritis and osteoporosis, collagen hydrolysate is of interest. Its excellent safety makes it attractive as a treatment for many chronic health conditions [63].

Hydrolyzed collagen has a strong therapeutic role in osteoporosis and osteoarthritis, with the potential to increase the amount of minerals in bone tissues, protect articular cartilage, and, most importantly, relieve pain symptoms [5]. Guillerminet et al. [64] reported that the growth and differentiation of both osteoblasts and osteoclasts increased significantly, and an osteoprotective effect was noted. Additionally, daily doses of 12 g significantly enhanced the symptoms of osteoarthritis and osteoporosis. However, further

Table 3
Application of Collagen Hydrolysate as a Biomaterial, Modified from (León-López et al., 2019).

Product	Functionality	Reference
Cellulose–Hydrolyzed collagen films	High capacity for absorbing UV radiation and promoting cell adhesion and proliferation, as well as being biocompatible.	[57]
Cellulose–Hydrolyzed collagen films	Excellent protection against UV light	[58]
Hydrolyzed collagen biomaterial	treat bone and joint problems	[59]
Hydrolyzed collagen-chitosan sponges	Excellent biocompatibility and antimicrobial action, as well as good water uptake capacity	[31]
Hydrolyzed collagen hydrogels	Good drug release in acidic pH and low water absorption	[60]
Hydrolyzed collagen-chitosan hydrogels	Antibacterial capacity against *Escherichia coli* and *Staphylococcus aureus*	[56]
Nanofibrous scaffold prepared with Hydrolyzed collagen	Antimicrobial property against *E. coli* and *Pseudomonas aeruginosa*	[61]

research is required to determine the factors that cause osteoporosis and osteoarthritis, how to diagnose them early, and when to begin supplement consumption, as well as the appropriate dosage, to achieve worthy therapeutic goals [64].

6.3. Effect on heart health

Sclerosis (hardening of artery walls) is caused by the fragmentation of elastin, which leads to an increase in collagen fibers and smooth muscle cells. This calcification causes the blood vessel walls to become harder. To limit the risk of significant cardiovascular illnesses, arteriosclerosis should be assessed using morphological and functional techniques at an early stage. The balance between the two cholesterol types linked to cardiovascular diseases is shown by the low-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (LDL-C/HDL-C ratio). Additionally, when the LDL/HDL-C ratio exceeds 2.5, the plaque area grows quickly. A functional food made from collagen called collagen tripeptide (CTP) has several tripeptides with the Gly-X-Y sequence. When CTP is given orally to hypercholesterolemic rabbits, the amount of total cholesterol in their serum, the size of their atherosclerotic plaques, and the number of macrophages and smooth muscle cells are decreased [65].

Collagen provides arterial structure so that blood can flow freely to and from the heart. Collagen supplements have been shown in studies to reduce arterial stiffness and increase good HDL cholesterol levels in the body. This means it may lower your chances of developing coronary disease. A study showed that the collagen tripeptide appears to help prevent and treat atherosclerosis in healthy humans, the ratio of low-density lipoprotein cholesterol (LDL-C) to high-density lipoprotein cholesterol (HDL-C) was significantly reduced, and a significant decrease in toxic advanced glycation end products (TAGEs), which are used as an indicator of the development of atherosclerosis caused by dysfunctional glucose metabolism, was shown [7].

6.4. Effect on wound Healing and repair

The oral intake of collagen improved wound healing. Collagen-based dressings have been shown to improve wound healing in diabetic foot ulcers and burns in previous studies. Collagen dressings have been suggested as a way to reduce bacterial burden, protect growth factors from proteases, decrease matrix metalloproteinases, boost cell proliferation and the synthesis of new tissues, and neutralize free radicals. Experimental studies have also shown that the ingestion of 2 g of hydrolyzed collagen per kilogram of body weight improves wound healing in diabetic ulcers and contributes to reduced inflammation and faster tissue repair [8]. In men with a 2030 % burn, a study revealed that taking hydrolyzed collagen-based supplements for four weeks significantly improved the serum prealbumin concentration and wound healing rate. Clinically, the decrease in hospital stay time was also critical [8].

6.5. Antioxidant and anti-inflammatory effect of hydrolyzed collagen

The use of collagen from different sources in tissue engineering and wound repair has received much attention. Collagen peptides are bioactive substances that improve skin physiology while also acting as safe functional food ingredients [66].

Milkfish are highly prized seafood, and their output rates have been increasing annually. To reduce pollution and increase the value of byproducts, many fish scales can be transformed into beneficial collagen peptides. A study that used milkfish collagen peptide (MSCP) prepared by pepsin-soluble collagen hydrolysis to demonstrate its antioxidant and anti-inflammatory activities revealed that MSCP has antioxidant, anti-inflammatory, and DNA-protective properties and is safe. MSCP can reduce ROS by scavenging DPPH and generating ABTS radicals. The anti-inflammatory effect of MSCP was dose dependent and helped to protect DNA from UV and H_2O_2 damage. MSCP can thus be used as a cosmeceutical, tissue engineering agent, and health food additive because of its lack of cytotoxicity [66,67].

The ROS reduction and radical scavenging assays DPPH and $ABTS^+$ were used to measure the antioxidant activity of the MSCPs. The findings of Chen's study revealed that the antioxidant activity of MSCP was substantial. DPPH and $ABTS^+$ were scavenged by MSCP in a dose-dependent manner. MSCP (1 mg/mL) inhibited 50 % of the DPPH radical. The addition of DPPH radicals was completely stopped when the MSCP concentration was increased to 10 mg/mL. Moreover, MSCP dramatically reduced the activity of $ABTS^+$. After treatment with 0.5 mg/mL MSCP, an ABTS + scavenging rate greater than 80 % was attained [66].

According to earlier studies, antioxidant peptides have anti-inflammatory properties. Leukotrienes, which act as mediators of a number of inflammatory and allergic diseases, are produced in large part by the enzyme lipoxygenase [68]. An inflammatory response mediator and regulator is NO. Hence, the level of inflammation can be assessed by reducing NO and lipoxygenase activity. MSCP had dose-dependent anti-inflammatory effects. The findings of Chen's study from 2018 are in line with those of studies on bioactive peptides derived from marine resources. The ability of the amino and hydroxyl groups of collagen peptides to combine with nitric oxide radicals and the enzyme lipoxygenase, respectively, may be the cause of their inhibition, which this report relates to the anti-inflammatory properties of MSCP [66,68].

Biomolecule oxidation is a free radical-mediated process that alters the flavor, texture, and aesthetic appeal of food. Degenerative illnesses such as cancer, neurological diseases, aging-related ailments, and diabetes can all be caused by free radicals. As a result, it is critical to prevent the production of free radicals in both food and living organisms [69]. Using double enzymatic hydrolysis, three novel collagen peptides with different molecular weights were extracted from cowhide collagen, and their antioxidant activity and functional characteristics were investigated. The following ideal enzymatic hydrolysis conditions were used to produce CCAPs with the maximum DPPH scavenging rate: 1.5 h, 55 °C, pH 7.4, and a neutral enzyme-to-trypsin ratio of 0.048:0.016. The hygroscopicity (HYG), oil holding capacity (OHC), and water holding capacity (WHC) of the CCAPs significantly increased as the molecular weight decreased. Nevertheless, CCAP-II has excellent emulsifying characteristics, whereas CCAP-I has outstanding foaming properties, and

CCAP-III demonstrated the best antioxidant efficacy. These substances are also known as functional agents or antioxidants because of their excellent antioxidative activity [69].

6.5.1. Future research development

In 2021, the global collagen market size was USD 8680 million, and it is expected to grow to USD 19,167 million during the period 2022–2030. The diversity in its functions and natural occurrence has made collagen clinically versatile and convenient for different nonfood and food applications, which has driven the market to profit from the growing prevalence of collagen-based products. Since populations are increasing worldwide, consumers are also driven to adopt such products [10].

An analysis by Data Bridge Market Research showed that the hydrolyzed collagen market is expected to reach USD 1882.37 million by 2030, which was USD 1174.80 million in 2022, indicating a CAGR of 6.07 % during the forecast period of 2023–2030. In addition to insights into market scenarios such as market value, growth rate, segmentation, geographical coverage, and major players, the market reports curated by the Data Bridge Market Research also include in-depth expert analysis, geographically represented company wise production and capacity, network layouts of distributors and partners, detailed and updated price trend analysis and deficit analysis of supply chains and demand [70].

Enzymatic hydrolysis in batch reactors produces hydrolyzed collagen at a controlled pH and temperature. Batch reactors, on the other hand, have several disadvantages, including low efficiency and productivity because the enzyme is utilized only a single time, variability in product quality and attributes due to batch-to-batch differences, and time-wasting, which also contribute to reduced productivity, large space requirements, and the inability to procure the final product immediately and continuously. Many of these issues were solved with the creation of the Enzymatic Membrane Reactor (EMR). The use of EMR allows for the fractionation of hydrolyzed peptides to produce different fractions with different molecular weight distributions, allowing for a wider range of applications [24].

Agrofood waste can be used to produce hydrolyzed collagen (bones, skin, and tendons). Recycling these byproducts and turning them into new products with high functional value can help decrease the pollution that these wastes produce. Traditionally, acids or alkaline products have been used to denature collagen; however, a combination of elevated temperatures and pressures, as well as high-intensity ultrasound, have been examined as innovative approaches to minimize the use of these chemical products [29].

Recent research has focused on new collagen sources, including the placenta of cattle or human placenta. Placenta extract is already used in the formulation of many cosmetics and is also of interest as a source of different bioactive compounds. Collagen and its byproducts can be used for wound healing, especially because the wound healing effect of placenta extract is well known due to its cleansing, anti-inflammatory and antimicrobial properties [71]. In parallel, research on collagen hydrolysate is considered very broad in terms of five aspects: processing technologies, targeted receptors, diseases, types of collagen and species. Scientists have investigated novel sources of collagen hydrolysate Type I and Type II, especially those extracted by both chemical and enzymatic hydrolysis [72].

7. Summary and concluding remarks

Hydrolyzed collagen HCs remain nonviscous in aqueous solutions, are odorless and transparent in color, can act as emulsifiers and stabilizers, and can form films and foams. HC has good wettability and solubility, dispersibility, a carrier capacity with low allergenicity, antioxidant and antimicrobial activity, and high biocompatibility and biodegradability. Hydrolyzed collagen has effective biological effects, such as increasing cell proliferation and water-holding capacity. Because of its properties, it is widely accepted for use as a functional and effective ingredient in the food-service, pharmaceutical, and cosmetics industries. It improves the sensorial qualities and enhances the physical and chemical characteristics of food and beverage products. The use of HC combined with biopolymers such as chitosan or cellulose for the preparation of scaffolds in the biomedical industry helps in collagen synthesis, bone and joint condition management, wound and damaged tissue healing, heart disease treatment, and skin aging slowing. The regular and daily intake of hydrolyzed collagen at various doses and from various sources has been shown to have numerous health benefits for the human body due to its antioxidant and anti-inflammatory effects. Hydrolyzed collagen can be extracted from bovine, porcine, chicken, and fish cartilage. It can be linked to vitamins and other kinds of nutrients and is easily consumed as a supplement or blended into a variety of food and beverages. HC has a wide assortment of purposes in the food industry and has a potential role in enhancing the physiochemical properties of many food products and treating skin and bone disorders.

Data availability

No data associated with our study has been deposited into a publicly available repository. This study primarily involved the synthesis and analysis of existing literature, and no new experimental data were generated.

No data was used for the research described in the article. This study is based on a comprehensive review and synthesis of existing literature, and therefore, no new data were generated or utilized.

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Walaa Al Hajj: Writing – original draft, Conceptualization. **Mohamed Salla:** Resources, Investigation, Data curation. **Maha Krayem:** Writing – review & editing, Validation, Resources. **Sanaa Khaled:** Writing – review & editing, Validation, Resources. **Hussein F. Hassan:** Validation, Methodology, Formal analysis. **Sami El Khatib:** Writing – original draft, Supervision, Project administration, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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